Eur J Vasc Endovasc Surg (2015) 49, 420–425

The Benefit of Revascularization in Nonagenarians with Lower Limb Ischemia is Limited by High Mortality

E. Saarinen *, **S. Vuorisalo, P. Kauhanen, A. Albäck, M. Venermo**

Department of Vascular Surgery, University of Helsinki and Helsinki University Hospital, Finland

WHAT THIS PAPER ADDS

The increased life expectancy of the population has led to new challenges, as very old patients with vascular problems are referred to vascular specialists. This series assesses the outcome of patients aged 90 years and older with lower limb ischemia. It was found that good limb salvage can be achieved by both surgical and endovascular revascularization, and independent living can be maintained in the majority of patients. However, the benefit of revascularization is limited by high mortality. Dementia seems to be an independent risk factor for poor survival, and in these patients conservative treatment should be considered if possible.

Objective/Background: Owing to the increased life expectancy of the population the number of very old patients referred to vascular surgical units has increased. Advanced age is a well known risk factor in patients undergoing surgical interventions for lower limb ischemia. However, amputation performed on an elderly person living independently will lead to permanent institutional care. The aim of this study was to evaluate the outcome of patients aged 90 years and older with lower limb ischemia undergoing surgical or endovascular revascularization.

Methods: Two hundred and thirty-three nonagenarians with either chronic critical limb ischemia (CLI) or acute limb ischemia (ALI) who underwent revascularization at the authors' institution between 2002 and 2013 were included in this retrospective study. Risk factors were evaluated and survival, limb salvage, and amputation free survival (AFS) assessed.

Results: The median age of the study population was 92 years (range 90–100 years). The majority (81.1%) of the patients were female. One in four (24.5%) patients had diabetes, and the incidence of coronary artery disease was 79.8%. Seventy-three percent of the patients had CLI and 27% of had ALI. Seventy percent of the patients underwent surgical revascularization and 30% were treated endovascularly. The majority (72.5%) of the patients maintained their independent living status; 27.5% ended up in institutional care post-operatively. Similarly, the majority (82.0%) of the patients maintained their walking ability, while 18% were not able to ambulate independently after revascularization. One year survival, limb salvage, and AFS rates were 50.9% versus 48.6% ($p = .505$), 85.1% versus 87.0% ($p = .259$), and 45.7% versus 44.4% ($p = .309$) in the surgical versus endovascular group, respectively. Dementia was an independent risk factor of poor AFS (odds ratio: 1.56; 95% confidence interval: 1.077–2.272; $p = .019$).

Conclusion: Good limb salvage can be achieved by both surgical and endovascular revascularization, and independent living can be maintained in the majority of the patients. However, the benefit of revascularization is limited owing to high mortality, especially in patients with dementia.

Article history: Received 2 September 2014, Accepted 23 December 2014, Available online 16 February 2015

Keywords: Lower limb ischemia, Nonagenarians, Outcome, Revascularization

INTRODUCTION

As a result of increasing life expectancy, older patients with lower limb ischemia are being referred to vascular surgery units.[1] Revascularization of a critically ischemic leg can be justified for very elderly patients because limb preservation is likely to maintain ambulatory status and independent living.[2–4] Good patency and limb salvage rates after infrainguinal bypass can be achieved in older patients.[5,6] However, the overall benefit from infrainguinal bypass may be limited in the very elderly because advanced age is associated with increased peri- and post-operative mortality after vascular operations.[7] Earlier data from the authors' institution demonstrated that in octogenarians with critical limb ischemia (CLI), endovascular revascularization was associated with better amputation free survival (AFS) than bypass.[8] Not only octogenarians, but also patients over 90 years of age are referred to vascular surgical units because

* Corresponding author.
E-mail address: eva.saarinen@hus.fi (E. Saarinen).

http://dx.doi.org/10.1016/j.ejvs.2014.12.027

of chronic or acute lower limb ischemia. Yet the outcome for nonagenarians with lower limb ischemia is not well known. Therefore, the main aim of this study was to assess the outcome of nonagenarians with lower limb ischemia in terms of limb salvage, survival, and AFS. Secondary objectives were to assess the independence and functional outcome after the revascularization.

MATERIAL AND METHODS

Two hundred and thirty-three consecutive patients over 90 years of age who underwent either surgical or endovascular revascularization for lower limb ischemia between January 2002 and December 2012 at Helsinki University Central Hospital were included in this retrospective study. Demographic data, procedural details, post-operative outcome, and follow up data were collected prospectively into the authors' institutional vascular and endovascular database (Husvasc), and scrutinized retrospectively. The demographic data included age, sex, comorbid conditions (diabetes, coronary artery disease [CAD], hypertension, dyslipidemia, cerebrovascular disease, renal insufficiency), and smoking habits, as well as pre-operative ambulatory and living status. The procedural data contained indications, type of revascularization, and details of the treated arterial segment (inflow and outflow vessels, and target vessel of endovascular revascularization), as well as graft materials and balloons, stents and so on. Post-operative data included complications and outcome at discharge. The follow up data comprised post-operative ambulatory and living status, limb status, revascularization patency, and dates of major amputation or death. The date and cause of late death were retrieved from the Finnish national population register, Statistics Finland. Data on late major lower limb amputation were completed retrospectively from the amputation register.

Diabetes was considered as hyperglycemia requiring diet, oral medication, or insulin treatment. CAD was defined as a previously documented myocardial infarction and/or ongoing angina pectoris, or previous coronary bypass surgery or percutaneous coronary intervention. Cerebrovascular disease was defined as a previous stroke or transient ischemic attack. Estimated glomerular filtration rate (eGFR) was determined according to the modified Modification of Diet in Renal Disease study equation.[9,10] The presence of dementia was based on previously diagnosed dementia in patient records (Alzheimer's disease, vascular dementia, or other type of permanent cognitive impairment). The diagnosis was usually made by a neurologist or geriatrician. The functional status pre- and post-operatively was assessed as living status (home, nursing/sheltered home, healthcare center, or hospital) and as ambulatory status (walking without aid, walking stick, walking aid, wheelchair, or bedridden).

Survival, limb salvage, and AFS rates with mean ± SE were calculated by the Kaplan—Meyer method. Cox regression analysis was used to assess risk factors associated with poor AFS. All variables presented in Table 1, as well as revascularization level and type of ischemia (acute vs. chronic), were included in univariate analysis. Only variables with a p value < 0.2 in univariate analysis were included in regression model. Statistical analysis was performed using SPSS 19.0 statistical software (IBM, Armonk, NY, USA). The study protocol was approved by the institutional review board of Helsinki University Central Hospital (Department of Surgery).

Table 1. Demographic data of 233 nonagenarians undergoing revascularization for lower limb ischemia.

Demographics	*N*	%
Age (y), median (range)	92 (90—100)	
Sex		
Male	44	18.9
Female	189	81.1
Diabetes	57	24.5
CAD	186	79.8
Hypertension	176	75.5
Dyslipidemia	102	43.8
COPD	29	12.4
Current smoking	5	2.1
Cerebrovascular disease	37	15.9
Renal insufficiency	148	63.5
Mild—moderate (eGFR 30—60 mL/min/1.73 m^2)	131	56.2
Severe (eGFR $<$ 30 mL/min/1.73 m^2)	17	7.3
Dementia	43	18.5

Note. CAD = coronary artery disease; COPD = chronic obstructive pulmonary disease; eGFR = estimated glomerular filtration rate.

RESULTS

The median age of the study population was 92 years (range 90—100 years). The majority (81.1%) of the patients were female. The incidence of diabetes was 24.5%. Eighty percent of patients had CAD. There were only a few current smokers ($n = 5$; 2.1%). More than 60% (63.5%) of the patients had renal insufficiency; in most (56.2%), the renal insufficiency was mild or moderate (eGFR 30—60 mL/min/1.73 m^2), whereas 7.3% suffered from severe renal insufficiency (eGFR $<$ 30 mL/min/1.73 m^2). Almost one in five patients (18.5%) had dementia (Table 1).

Seventy-three percent ($n = 170$) of the patients had chronic CLI (rest pain $n = 56$, ulcer/gangrene $n = 114$) and 27% ($n = 63$) had ALI (thrombosis, embolism). Seventy percent of the patients underwent surgical revascularization (bypass, endarterectomy, or thrombectomy/embolectomy), and 30% were treated endovascularly. The type of revascularization is presented in detail in Fig. 1.

The overall survival, limb salvage, and AFS at 1 year were 50.2%, 85.8%, and 45.5%, respectively. The median survival time was 12.3 months (range 0—152.0 months), and 5 year survival was 13.2%. The overall peri-operative (30-day) mortality was 16.7% (19.6% vs. 10% in the surgical vs. endovascular group [$p = .505$], respectively). The respective 1 year survival, limb salvage, and AFS rates were 50.9% versus 48.6% ($p = .505$), 85.1% versus 87.0% ($p = .259$), and 45.7% versus 44.4% ($p = .309$) in the surgical versus

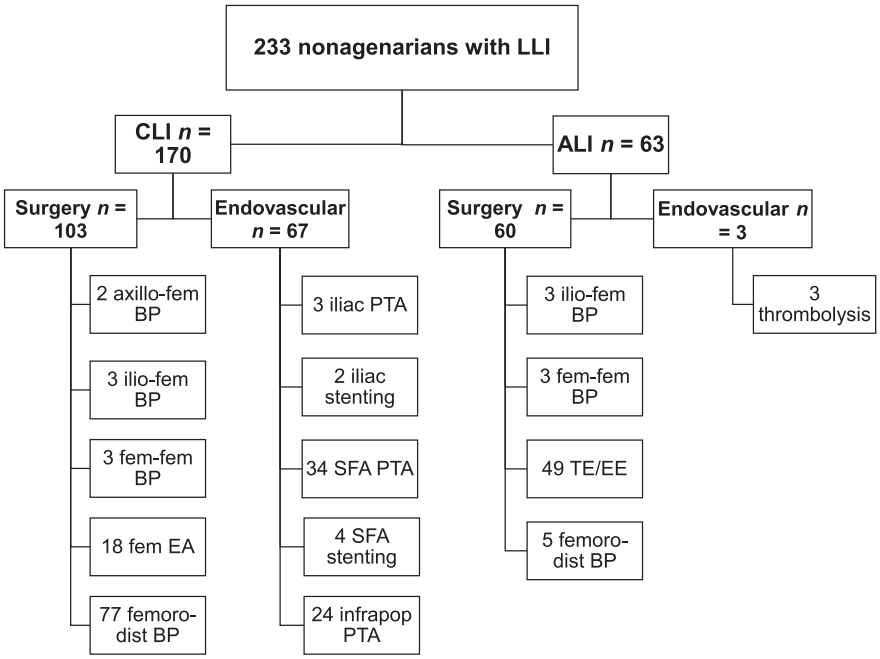

Figure 1. Revascularization details of study population. *Note*. LLI = lower limb ischemia; CLI = chronic critical limb ischemia; ALI = acute limb ischemia; BP = bypass; EA = endarterectomy; PTA = percutaneous transluminal balloon angioplasty; TE = thrombectomy; EE = embolectomy; fem = femoral; infrapop = infrapopliteal.

endovascular group, respectively. When the outcome of CLI versus ALI was compared, there was no statistically significant difference in limb salvage at 1 year (85.8% vs. 82.9%; $p = .332$). One year survival and AFS were better in the CLI group (57.1% vs. 31.7% [$p = .007$] and 51.2% vs. 30.2% [$p = .015$]). In Cox regression analysis, dementia was the only independent risk factor of poor AFS (odds ratio: 1.56; 95% confidence interval: 1.077—2.272; $p = .019$) (Table 2; Fig. 2)

Pre-operatively 83% ($n = 194$) of the patients were living at home or in home like circumstances (nursing home or sheltered home), and the majority (72.2%) of these patients maintained their independent living status, whereas 27.8% ended up, at least temporarily, in institutional care post-operatively (Fig. 3). There was no statistically significant difference between surgically and endovascularly treated patients regarding the preservation of pre-operative living status (71.2% vs. 75.7%, respectively; $p = .476$). Ninety-one percent ($n = 213$) of the patients were ambulatory pre-operatively, and the majority (82.2%) of these patients maintained their walking ability, while 17.8% were not able to ambulate independently after revascularization (Fig. 4.) The preservation of ambulatory status did not differ between surgical and endovascular revascularization (81.0% vs. 84.3%, respectively; $p = .548$).

Table 2. Cox regression analysis of the predictors of poor amputation free survival.

	OR	95% CI	*p*
Dementia	1.560	1.077—2.272	.019
Diabetes	0.003	0.215—5.008	.956
Hypertonia	0.607	0.689—1.174	.436
Renal insufficiency	0.024	0.993—1.006	.878
Smoking	0.006	0.481—1.969	.940

Note. Variables presented in Table 1 with a *p*-value < .2 in univariate analysis were included in regression model. OR = odds ratio; CI = confidence interval.

DISCUSSION

The increased life expectancy of the population has led to new challenges as very old patients with vascular problems are referred to vascular specialists. In the future, the

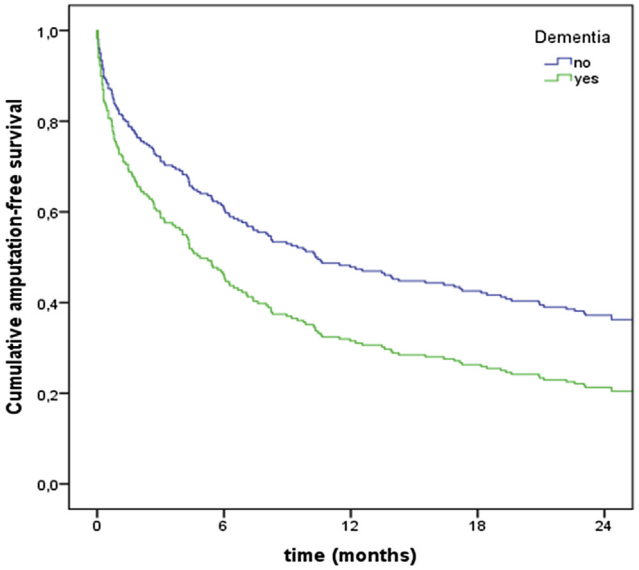

Figure 2. Dementia was an independent risk factor of poor amputation free survival (odds ratio: 1.56; 95% confidence interval: 1.077—2.272; $p = .019$).

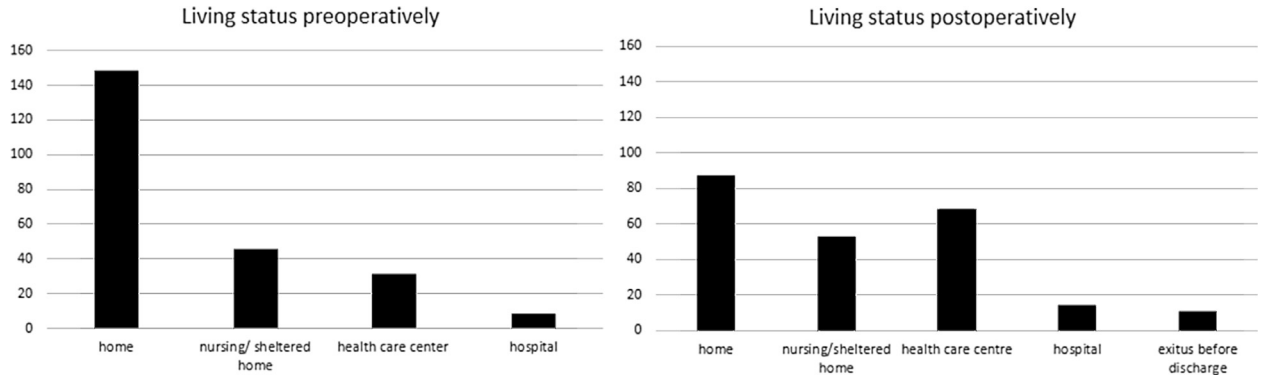

Figure 3. Living status pre-operatively and after revascularization.

number of nonagenarians and even older patients will increase. Therefore, a new problem is being faced—at what age does a patient cease to be a candidate for revascularization? This series assesses the outcome of the oldest patients with lower limb ischemia. It has been shown that in nonagenarians, the median survival was low. However, the limb salvage rate was good and the majority of the patients maintained their ambulatory status and independent living. For this patient group, it seems to be most important to assess frailty and cognition pre-operatively to predict adverse post-operative outcomes. This helps the clinician to choose the best treatment for each patient. Furthermore, the people taking care of these patients should be alerted to diagnose complications early.

Advanced age is definitely a risk factor in patients undergoing lower limb revascularization,[7] but it is difficult to determine a certain age limit for attempting revascularization. In the present series, the overall peri-operative mortality was 16.7% (19.6% vs. 10.0% in a surgical vs. endovascular group, respectively). Peri-operative mortality rates in series of octogenarians with CLI in the literature are reported to be 2—22% for patients undergoing infrainguinal bypass,[3,8,11—14] and 2—12% for those undergoing endovascular revascularization.[3,5,6,8,12,13,15] Therefore, it seems that there is no significant difference between octogenarians and nonagenarians in terms of peri-operative mortality. However, as one might expect, the older the patients are, the shorter the life expectancy is. In the current series of nonagenarians, the median survival was only 12.3 months (0—152 months) and 5-year survival only 13.2%, which is a much poorer rate than in an earlier series of octogenarians with CLI, in which the median survival time was 2.5 years and 5 year survival was 35.7%.[8] Considering this, conservative treatment, at least in patients with limited tissue loss and tolerable rest pain, might be the best option. Although the prognosis of unreconstructable CLI is poor, in this particular patient group, the 54% limb salvage and 46% survival rate at 1 year described by Lepäntalo and Mätzke can be considered acceptable.[16] However, in this age group, long-term survival is perhaps not the most appropriate end point. A more relevant one might be that the majority of these patients preserved their limb and were able to live the rest of their lives independently in their own home. It is therefore clear that among patients over 90 years of age, only those with such expectations should be considered for revascularization. Moreover, age per se is not the only determinant of poor outcome in this very elderly patient group. Comorbid conditions, the suitability of arterial anatomy for revascularization, and other patient related factors are even more important to take into consideration than in younger patients. The current series also included patients with acute lower limb ischemia. Limb salvage at 1 year (82.9%) was the same as patients with CLI, but 1 year mortality was significantly higher in patients with ALI. Similarly, Galzerano et al. published a good 1 year limb salvage rate (88.2%) in nonagenarians with acute limb ischemia,[17] but concluded that in this patient group vascular procedures are associated with high mortality.

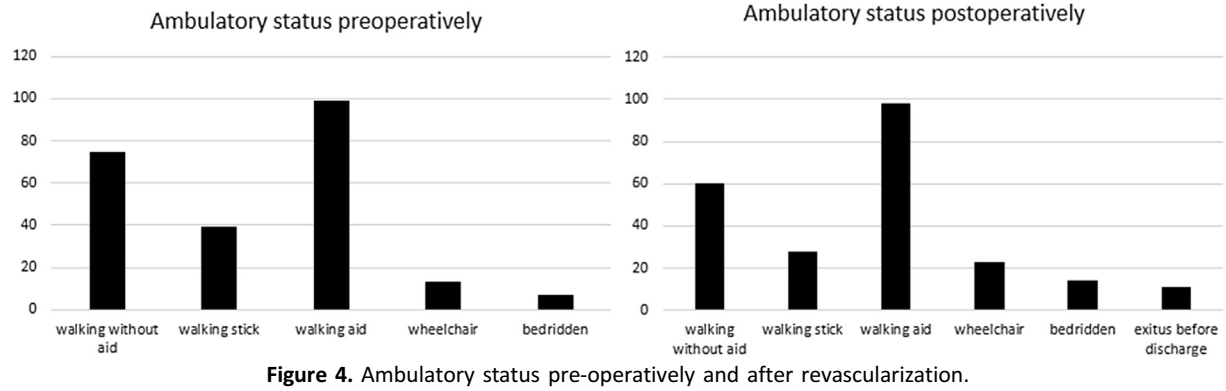

Figure 4. Ambulatory status pre-operatively and after revascularization.

The results of this study show a trend towards better peri-operative survival in the endovascular group. A similar finding has been described in a series of octogenarians.[6,8] However, at 1 year limb salvage and AFS were similar in the surgical versus endovascular groups. The impairment of living status and ambulatory status after revascularization were also similar between the two treatment methods. Although endovascular revascularization is considered less invasive, in this series of nonagenarians, the endovascular approach did not have any benefit over surgery in terms of preserving functional status. A similar finding was observed recently by Vogel et al.[18]

The patient demographics of nonagenarians differ quite significantly from those usually reported in series of patients with CLI. In this age group, patients were predominantly (81%) female, and only 25% had diabetes. The low incidence of diabetes in this age group is probably due to the high mortality and reduced life expectancy of diabetics with severe peripheral arterial disease.[19] However, the incidence of CAD (80%) and renal insufficiency (64%) were extremely high. In the present series, dementia was the only significant predictor of poor survival. Similar findings were shown by Hu et al.,[20] where dementia patients who underwent surgery had a significantly higher overall post-operative complication rate compared with controls. Patients with dementia had a higher incidence of acute renal failure, pneumonia, septicemia, stroke, and urinary tract infection. These complications were difficult to diagnose in their initial stages because the symptoms differ from the usual, which may delay diagnosis.

Cognitive impairment predominates in the older population. Patients with dementia often have comorbid conditions that may lead to post-operative mortality and morbidity. The incidence of delirium is high in older, frail surgical patients, especially if dementia or cognitive decline is present.[21] The prognosis of delirium is extremely poor, leading to permanent institutionalization and high mortality.[22] Patients with dementia and decreased cognitive reserve need a lower number of etiologies to develop delirium and the profile of causative agents differs among patients with and without dementia.[23] Patients undergoing vascular surgery are prone to delirium.[24] Elderly patients have physiological changes that impair the functional reserve and increase vulnerability to disability. Dementia is much more than a memory and cognitive dysfunction. The concept of frailty has been developed to characterize decreased physiological reserves across multiple organ systems arising from cumulative comorbid conditions.[25]

Risk factors for peripheral vascular disease, such as hypertension, hypercholesterolemia, and smoking, predispose to vascular cognitive impairment and increase the risk of delirium. The prevalence of undiagnosed cognitive impairment in older patients presenting for vascular surgery has been investigated by Partridge et al.[26] According to their study, the prevalence of cognitive impairment among older patients (>60 years) is high (68%) and frequently undiagnosed (88.3%) before admission. They suggest the identification of cognitive impairment pre-operatively as the combined assessment of frailty and cognition is predictive of adverse post-operative outcomes and longer hospital stay. In this study, 18.5% of patients had been diagnosed with dementia or cognitive impairment. However, according the results of Partridge et al.,[26] the prevalence of dementia should have been much higher. The underestimation of the presence of dementia in the current study is probably due to the fact that the diagnosis of dementia was dependent on previous diagnosis by neurologist or geriatrician, and no formal mental or cognitive assessment was performed pre-operatively.

The limitations of the study are its retrospective setting and the lack of a control group. One flaw is also the heterogeneity of the study population as the study included patients with both chronic and acute presentations of limb threatening ischemia. The inclusion of acute cases is relevant as this pattern appears to become more frequent with increasing age.

In conclusion, the overall survival of patients aged 90 years and older is very poor. Good limb salvage can be achieved by both surgical and endovascular revascularization and independent living can be maintained in the majority of patients. However, the benefit of revascularization is limited by high mortality. Dementia seems to be an independent risk factor for poor survival, and in these patients conservative treatment should be considered if possible.

CONFLICT OF INTEREST

None.

FUNDING

None.

REFERENCES

1 Diehm C, Schuster A, Allenberg JR, Darius H, Haberl R, Lange S, et al. High prevalence of peripheral arterial disease and co-morbidity in 6880 primary care patients: cross sectional study. *Atherosclerosis* 2004;**172**:95—105.
2 Luther M, Lepäntalo M. Femorotibial reconstructions for chronic critical leg ischaemia: influence on outcome by diabetes, gender and age. *Eur J Vasc Endovasc Surg* 1997;**13**:569—77.
3 Pomposelli Jr FB, Arora S, Gibbons GW, Frykberg R, Smarowski P, Campbell DR, et al. Lower extremity arterial reconstruction in the very elderly: successful outcome preserves not only limb but also residential status and ambulatory function. *J Vasc Surg* 1998;**28**:215—25.
4 Zdanowski Z, Troeng T, Norgren L. Outcome and influence of age after infrainguinal revascularisation in critical limb ischemia. The Swedish Vascular Registry. *Eur J Vasc Endovasc Surg* 1998;**16**:137—41.
5 Chang JB, Stein TA. Infrainguinal revascularization in octogenarians and septuagenarians. *J Vasc Surg* 2001;**34**:133—8.
6 Brosi P, Dick F, Do DD, Schmidli J, Baumgartner I, Diehm N. Revascularization for chronic critical lower limb ischemia in octogenarians is worthwhile. *J Vasc Surg* 2007;**46**:1198—207.
7 Plecha FR, Bertin VJ, Plecha EJ, Avellone JC, Farrel CJ, Hertzer NR, et al. The early results of vascular surgery in

patients 75 years of age or older: an analysis of 3259 cases. *J Vasc Surg* 1985;**2**:769—74.
8 Arvela E, Venermo M, Söderström M, Korhonen M, Halmesmäki K, Albäck A, et al. Infrainguinal percutaneous transluminal angioplasty or bypass surgery in patients aged 80 years and older with critical limb ischemia. *Br J Surg* 2011;**98**:518—26.
9 Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. *Ann Intern Med* 1999;**130**:461—70.
10 Levey AS, Coresh J, Greene T, Stevens LA, Zhang YL, Hendriksen S, et al. Using standardized serum creatinine values in the modification of diet in renal disease study equation for estimating glomerular filtration rate. *Ann Intern Med* 2006;**145**:247—54.
11 O'Mara CS, Kilgore Jr TL, McMullan MH, Maples MD, Hollingsworth JF, Tyler HB. Distal bypass for limb salvage in very elderly patients. *Am Surg* 1987;**53**:66—70.
12 Scher LA, Veith FJ, Ascer E, White RA, Samson RH, Sparayregen S, et al. Limb salvage in octogenarians and nonagenarians. *Surgery* 1986;**99**:160—5.
13 Doslouglu HH, Lall P, Cherr GS, Harris LM, Dryjski ML. Superior limb salvage with endovascular therapy in octogenarians with critical limb ischemia. *J Vasc Surg* 2009;**50**:305—15.
14 de Leur K, van Zeeland M, Ho G, de Groot H, Veen E, van der Laan L. Treatment for critical lower limb ischaemia in elderly patients. *World J Surg* 2012;**36**:2937—43.
15 Salas CA, Adam DJ, Papavassiliou VG, London NJM. Percutaneous transluminal angioplasty for critical limb ischemia in octogenarians and nonagenarians. *Eur J Vasc Endovasc Surg* 2004;**28**:142—5.
16 Lepäntalo M, Mätzke S. Outcome of unreconstructed chronic critical leg ischaemia. *Eur J Vasc Endovasc Surg* 1996;**11**:153—7.
17 Galzerano G, de Donato G, Setacci F, Sirignano P, Sauro L, Cappelli A, et al. Acute limb ischaemia in nonagenarians. *J Cardiovasc Surg (Torino)* 2013;**54**:625—31.
18 Vogel T, Petroski G, Kruse R. Functional status of elderly adults before and after interventions for critical limb ischaemia. *J Vasc Surg* 2014;**59**:350—8.
19 Faglia E, Clerici C, Clerissi J, Gabrielli L, Losa S, Mantero M, et al. Long-term prognosis of diabetic patients with critical limb ischaemia: a population-based cohort study. *Diabetes Care* 2009;**32**:822—7.
20 Hu CJ, Liao CC, Chang CC, Wu CH, Chen TL. Post-operative adverse outcomes in surgical patients with dementia: a retrospective cohort study. *World J Surg* 2012;**36**:2051—8.
21 de Castro SM, Ünlü Ç, Tuynman JB, Honig A, van Wagensveld BA, Steller EP, et al. Incidence and risk factors of delirium in the elderly general surgical patient. *Am J Surg* 2014;**208**:26—32.
22 Pitkala KH, Laurila JV, Strandberg TE, Tilvis RS. Prognostic significance of delirium in frail older people. *Dement Geriatr Cogn Disord* 2005;**19**:158—63.
23 Hölttä EH, Laurila JV, Laakkonen ML, Strandberg TE, Tilvis RS, Pitkala KH. Precipitating factors of delirium: stress response to multiple triggers among patients with and without dementia. *Exp Gerontol* 2014;**59**:42—6.
24 Böhner H, Hummel TC, Habel U, Miller C, Reinbott S, Yang Q, et al. Predicting delirium after vascular surgery: a model based on pre- and intra-operative data. *Ann Surg* 2003;**238**:149—56.
25 Fried LP, Ferrucci L, Darer J, Williamson JD, Anderson G. Untangling the concepts of disability, frailty, and comorbidity: implications for improved targeting and care. *J Gerontol A Biol Sci Med Sci* 2004;**59**:255—63.
26 Partridge JS, Dhesi JK, Cross JD, Lo JW, Taylor PR, Bell R, et al. The prevalence and impact of undiagnosed cognitive impairment in older vascular surgical patients. *J Vasc Surg* 2014;**60**(4):1002—11.